



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/773,866	02/01/2001	David Thomas	TNX00-03	3286

26839 7590 09/03/2002

TANOX, INC.
10301 STELLA LINK
HOUSTON, TX 77025

EXAMINER

GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
----------	--------------

1644

DATE MAILED: 09/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/773866	Applicant(s) THOMAS ET AL.	
	Examiner GAMBEL	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 7/15/02

2a) ☐ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) _____ is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on 7/15/02 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input checked="" type="checkbox"/> Other: <u>NOTICE TO COMPLY WITH SEQUENCE RULES</u>
---	--

7

DETAILED ACTION

1. Applicant's amendment, filed 7/15/02 (Paper No. 6), has been entered. Claims 6, 7 and 9 have been amended.
2. Applicant's election of Group I (claims 1-16) in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 17-20 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected invention and/or species; the requirement having been traversed

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant has not satisfied the requirement for the disclosure of sequences on page 9, paragraph 2 of the instant specification.

Applicant is reminded to amend the specification and/or the claims to specify the appropriate SEQ ID NOS., if appropriate.

Applicant is reminded of the sequence rules which require a submission for all sequences of more than 9 nucleotides or 3 amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

4. Upon a review of the instant application, page 19, line 2 discloses Table 1 and page 22, line 14 discloses Table 2, however Tables 1 and 2 do not appear in the specification as filed.

Applicant is required to address the disclosure of Tables in the specification as filed in the absence of Tables.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

6. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

7. Formal drawings, filed 7/15/02 have been submitted which fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may **NOT** be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

8. The application is required to be reviewed and all spelling, **TRADEMARKS**, and like errors corrected.

Trademarks should be capitalized or accompanied by the TM or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Again, applicant is to amend the specification and/or the claims to specify the appropriate **SEQ ID NOS.**, if appropriate.

Appropriate corrections are required

9. The filing date of the instant claims is deemed to be the filing date of instant application USSN 09/773,866, i.e. 2/1/01. Priority application USSN 60/178,934 does not support the broader claims of the instant application. For example, it does not appear that USSN 60/178,934 does not provide written support "non-professional human APCs", "induce phenotypical and functional maturation of monocyte derived dendritic cells" as well as all of the limitations of instant claims 6 and 7. If applicant desires priority prior to 2/1/01; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

10. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claims 1-9 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description encompassing "agonist anti-CD40 molecules" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies (see claim 13) because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of molecules other than agonist anti-CD40 antibodies as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" are not set forth in the specification as filed, commensurate in scope with the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

It appears that pages 9-10 of the instant specification relies upon screening and isolating non-antibody molecules from compound or peptide libraries. However, there is no disclosure of such non-antibody molecules encompassed by the claimed invention.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of antibody species to support an entire genus of non-antibody agonist anti-CD40 molecules. The instant invention encompasses any "agonist anti-CD40 molecule" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies"; yet the instant specification does not provide sufficient written description as to the structural features of said molecule other than anti-CD40 antibodies and the correlation between the chemical structure and the function of the genus of "molecules". The reliance on the disclosed limited examples of certain anti-CD40 agonist antibodies in the specification as filed does not support the written description of any "molecule" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies". It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological and pharmacological properties. Therefore, structurally unrelated "molecules" encompassed by the claimed invention other than agonist anti-CD40 antibodies would be expected to have greater differences in their structures and activities.

A person of skill in the art would not know which sequences (or chemical structures) are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences for identifying an agonist anti-CD40 molecule or "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies", encompassed by the claimed invention. There is insufficient guidance based on the reliance of agonist anti-CD40 antibodies to direct a person of skill in the art to select or to predict particular sequences as essential for identifying "agonist anti-CD40 molecules" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies", encompassed by the claimed invention.

The specification does not disclose nor identify "anti-CD40 molecules" or "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" other than anti-CD40 antibodies and CD40-binding fragments thereof.

"Molecules" including "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" differ in structure and physicochemical properties, which do not share critical common structural attributes. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "molecules" including "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" of which do not share critical common structural attributes; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

12. Claims 1-9 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "agonist anti-CD40 antibodies" and "CD40 binding fragments thereof" as disclosed in the specification as filed, does not reasonably provide enablement for any "agonist anti-CD40 molecule" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, chemical structure, etc.) that distinctly identifies the "agonist anti-CD40 molecules" and "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" other than those encompassed by the disclosure of "agonist anti-CD40 antibodies" and "CD40 binding fragments thereof" disclosed in the specification as filed. "Agonist anti-CD40 molecule" and "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" may have some notion of the activity of the claimed molecules, but fails to distinctly enable how to make and use the scope of "molecules" encompassed by the claimed invention. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "agonist anti-CD40 molecule" and "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies".

It appears that pages 9-10 of the instant specification relies upon screening and isolating non-antibody molecules from compound or peptide libraries. However, there is no disclosure of such non-antibody molecules encompassed by the claimed invention.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of antibody species to support an entire genus of non-antibody agonist anti-CD40 molecules. The instant invention encompasses any "agonist anti-CD40 molecule" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies"; yet the instant specification does not provide sufficient written description as to the structural features of said molecule other than anti-CD40 antibodies and the correlation between the chemical structure and the function of the genus of "molecules".

The reliance on the disclosed limited examples of certain anti-CD40 agonist antibodies in the specification as filed does not support the written description of any "molecule" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such anti-CD40 antibodies, encompassed by the claimed invention. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological and pharmacological properties. Therefore, structurally unrelated "molecules" encompassed by the claimed invention other than agonist anti-CD40 antibodies would be expected to have greater differences in their structures and activities.

A person of skill in the art would not know which sequences (or chemical structures) are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences for identifying an agonist anti-CD40 molecule or "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies", encompassed by the claimed invention. There is insufficient guidance based on the reliance of agonist anti-CD40 antibodies to direct a person of skill in the art to select or to predict particular sequences as essential for identifying "agonist anti-CD40 molecules" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies", encompassed by the claimed invention.

The specification does not disclose nor identify "anti-CD40 molecules" or "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" other than anti-CD40 antibodies and CD40-binding fragments thereof.

"Molecules" including "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies" differ in structure and physicochemical properties, which do not share critical common structural attributes.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. agonist anti-CD40 molecule) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single class of molecules (anti-CD40 antibodies) and, in turn, utilizing predicted structural determinations to ascertain binding or functional aspects of "agonist anti-CD40 molecules" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies", encompassed by the claimed invention and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Because of the lack of sufficient guidance and predictability in determining which structures would lead to "agonist anti-CD40 molecules" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies", with the desired properties and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of "agonist anti-CD40 molecules" encompassed by the claimed invention.

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

The success of state of the art structure-based strategies for inhibitor design is highly unpredictable. For example, Kuntz, Science (1992) 257:1078-1081 on page 1080, column 3, discloses that as little as 2% of compounds predicted to inhibit specific enzymatic or receptor systems actually show inhibition in the micromolar range. Kuntz further discloses that "optimization" of these compounds has proven even more problematic.

In the absence of sufficient guidance and direction to the structural and functional analysis, applicant's reliance upon a certain class of "agonist anti-CD40 antibodies" disclosed as filed does not appear to provide sufficient enabling support for any "agonist anti-CD40 molecules" as well as "analogues or homologues thereof or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies", encompassed by the claimed invention and so the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

13. Claims 1-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 1 and dependent claims thereof are objected to in that the "APCs" should be spelled out for at least the first time recited in the claims for clarity.

B) Claims 1-16 are indefinite in the recitation of "non-professional APCs" because the metes and bounds of said cells are ambiguous and indefinite. The specification does not appear to define this phrase nor sets for the metes and bounds of said cells.

C) For consistency and proper antecedent basis for claims 6-9, the recitation of "agonistic" in claim 4 should be amended to "agonist".

D) Claims 12, 13 and 16 contain the trademark or trade name "Delimmunized™". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 USC 112, second paragraph. See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark or the trade name "Delimmunized™" is used to identify or describe a product or possibly a product-by-process, and accordingly, the identification or the description is indefinite. The relationship between a trademark or tradename and the product it identifies may be uncertain and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark or tradename.

E) Claims 13-16 lack proper antecedent basis for "fragments".

Further, it is noted that given that hybridomas do not produce the antibody "fragments", applicant is invited to clarify rather the cell lines recited in claims 15-16 produce "fragments" or not.

F) Claim 13 lacks proper antecedent basis for the recitation of "or a peptide, oligonucleotide, peptidomimetic or an organic compound which binds to the same epitopes as such antibodies".

G) Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-6, 9 and 15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Caux et al. (Research in Immunology 145: 235-239, 1994) (see entire document).

Caux et al. teach functional CD40 on B lymphocytes and dendritic cells and that anti-CD40 antibodies can activate human progenitor and mature lymphocytes and dendritic cells (see entire document)

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced anti-CD40 antibodies, including The prior art agonist anti-CD40 antibodies would have had the inherent property of binding to and stimulating professional and non-professional antigen presenting cells, including dendritic cells as well as induce maturation of dendritic cells, encompassed by the claimed invention. Given this review of anti-CD40 antibodies, it would have been immediately apparent to the ordinary artisan at the time the invention was made that the teaching of said anti-CD40 antibodies would have produced by cell lines (e.g. hybridomas) that produced said anti-CD40 antibodies. Also, given the variety of anti-CD40 antibodies, Caux et al. teach anti-CD40 antibodies which can block CD40L:CD40 interactions and which can not block CD40:CD40L interactions.

17. Claims 1-6, 9 and 12-16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Armitage et al. (U.S. Patent No. 5,674,492) (1449) (see entire document).

Armitage et al. teach anti-CD40 antibodies, which have been demonstrated to exert costimulatory signals on normal B cells as well as the cell lines that produce said antibodies (see Background of the Invention)

Armitage et al. distinguish the prior art agonistic anti-CD40 antibodies from their disclosed M2/M3 antibodies which can inhibit binding of CD40 to CD40L (e.g. column 4, paragraph 2). It is noted that the M2/M3 antibodies can simulate B cells in contrast to its inhibitory effects on B cell lymphomas (e.g. Example 2 on column 13)

Armitage et al. teach that additional anti-CD40 antibodies may be generated by conventional techniques (e.g. column 5, paragraph 1) as well as the generation of recombinant antibodies and CD40 binding fragments thereof (e.g. columns 10-11, Additional CD40 Binding Proteins). Armitage teach the use of combinations of CD40 antibodies (e.g. Summary of the Invention).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced anti-CD40 antibodies, including the previously known anti-CD40 antibodies as well as the referenced Ms/M3 anti-CD40 antibodies. Given the expression of CD40 on various cell types, the prior art agonist anti-CD40 antibodies would have had the inherent property of binding to and stimulating professional and non-professional antigen presenting cells, including dendritic cells as well as induce maturation of dendritic cells, encompassed by the claimed invention.

18. Claims 1-6, 9 and 12-16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Fanslow et al. (U.S. Patent No. 5,801,227) (1449) (see entire document) alone and further evidence of Armitage et al. (U.S. Patent No. 5,674,492) (1449) (see Example 2, on column 13).

Fanslow et al. teach agonist anti-CD40 antibodies (see Background of the Invention), including monoclonal and recombinant antibodies as well as CD40 binding antibody fragments thereof for may uses as well as the cell lines that produce said antibodies (e.g. Background of the Invention and column 6, paragraph 4 - column 7, paragraph 3) (see entire document).

It is acknowledged that Fanslow's exemplified anti-CD40 antibodies can bind CD40 on CD40 bearing cells and block CD40 : CD40 L interactions.

Armitage et al. distinguish the prior art agonistic anti-CD40 antibodies from the M2/M3 antibodies which can inhibit binding of CD40 to CD40L (e.g. column 4, paragraph 2). It is noted that the M2/M3 antibodies can simulate B cells in contrast to its inhibitory effects on B cell lymphomas (e.g. Example 2 on column 13)

Given the expression of CD40 on various cell types, the prior art agonist anti-CD40 antibodies would have had the inherent property of binding to and stimulating professional and non-professional antigen presenting cells, including dendritic cells as well as induce maturaton of dendritic cells, encompassed by the claimed invention.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced anti-CD40 antibodies, including the previously known anti-CD40 antibodies as well as the referenced M2/M3 anti-CD40 antibodies.

19. Claims 1-4, 6 and 9 are rejected under 35 U.S.C. § 102(a)(b) as being anticipated by Zhou et al. (Hybridoma 18: 471 - 478, 1999) (see entire document). Zhou et al. teach agonist anti-human CD40 monoclonal antibodies that induces dendritic cell formation and maturation and the cell lines that produce said antibodies (see entire document, including Abstract, Materials and Methods, Results and Discussion).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced anti-CD40 antibodies.

Since there may be ambiguity over the priority of the instant claims, this rejection is made under 35 U.S.C. § 102(a)(b), as it would apply to the priority of the instant claims if applicant can provide appropriate written support and enablement for the instant or possibly amended claims. See the discussion above concerning priority of the instant claims.

20. Claims 1-9 and 12 are rejected under 35 U.S.C. § 102 (b) as being anticipated Katira et al. (Leukocyte Typing V, Schlossman et al. (Ed.), Oxford University Press, Oxford 1995, page 554). Katira et al. Teach the identification of co-operative epitopes on CD40 with anti-CD40 antibodies and combinations of anti-CD40 antibodies and that some of these antibodies block binding of CD40 to CD40L and some did not (see entire document).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced anti-CD40 antibodies. Given this review of anti-CD40 antibodies, it would have been immediately apparent to the ordinary artisan at the time the invention was made that the teaching of said anti-CD40 antibodies would have produced by cell lines (e.g. hybridomas) that produced said anti-CD40 antibodies.

21. Claims 1- 9 and 12-16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fanslow et al. (U.S. Patent No. 5,801,227) (1449) AND/OR Armitage et al. (U.S. Patent No. 5,674,492) AND/OR Zhou et al. (Hybridoma 18: 471 - 478, 1999) AND/OR Caux et al. (Research in Immunology 145: 235-239, 1994) AND/OR Katira et al. (Leukocyte Typing V, Schlossman et al. (Ed.), Oxford University Press, Oxford 1995, page 554) in view of the well known use of chimeric, humanized, Deimmunized, human antibodies at the time the invention was made, as acknowledged on page 6 - 9 of the instant specification.

Armitage et al. teach anti-CD40 antibodies, which have been demonstrated to exert costimulatory signals on normal B cells as well as the cell lines that produce said antibodies (see Background of the Invention)

Armitage et al. distinguish the prior art agonistic anti-CD40 antibodies from their disclosed M2/M3 antibodies which can inhibit binding of CD40 to CD40L (e.g. column 4, paragraph 2). It is noted that the M2/M3 antibodies can simulate B cells in contrast to its inhibitory effects on B cell lymphomas (e.g. Example 2 on column 13)

Armitage et al. teach that additional anti-CD40 antibodies may be generated by conventional techniques (e.g. column 5, paragraph 1) as well as the generation of recombinant antibodies and CD40 binding fragments thereof (e.g. columns 10-11, Additional CD40 Binding Proteins). Armitage teach the use of combinations of CD40 antibodies (e.g. Summary of the Invention).

Fanslow et al. teach agonist anti-CD40 antibodies (see Background of the Invention), including monoclonal and recombinant antibodies as well as CD40 binding antibody fragments thereof for may uses as well as the cell lines that produce said antibodies (e.g. Background of the Invention and column 6, paragraph 4 - column 7, paragraph 3) (see entire document).

It is acknowledged that Fanslow's exemplified anti-CD40 antibodies can bind CD40 on CD40 bearing cells and block CD40 : CD40 L interactions.

Armitage et al. distinguish the prior art agonistic anti-CD40 antibodies from the M2/M3 antibodies which can inhibit binding of CD40 to CD40L (e.g. column 4, paragraph 2). It is noted that the M2/M3 antibodies can simulate B cells in contrast to its inhibitory effects on B cell lymphomas (e.g. Example 2 on column 13)

Given the expression of CD40 on various cell types, the prior art agonist anti-CD40 antibodies would have had the inherent property of binding to and stimulating professional and non-professional antigen presenting cells, including dendritic cells as well as induce maturation of dendritic cells, encompassed by the claimed invention.

Zhou et al. teach agonist anti-human CD40 monoclonal antibodies that induces dendritic cell formation and maturation and the cell lines that produce said antibodies (see entire document, including Abstract, Materials and Methods, Results and Discussion).

Caux et al. teach functional CD40 on B lymphocytes and dendritic cells and that anti-CD40 antibodies can activate human progenitor and mature lymphocytes and dendritic cells (see entire document)

Katira et al. teach the identification of co-operative epitopes on CD40 with anti-CD40 antibodies and combinations of anti-CD40 antibodies and that some of these antibodies block binding of CD40 to CD40L and some did not (see entire document).

Fanslow et al., Armitage et al., Zhou et al., Caux et al. and Katira et al. differ from the claimed invention by not disclosing the well known use of Delmmunized and human antibodies at the time the invention was made. Zhou et al. and Caux et al. do not disclose the well known use of chimeric, humanized, Delmmunized, human antibodies at the time the invention was made. Fanslow et al., Armitage et al., Zhou et al. and Caux et al. differ from the claimed invention by not exemplifying combination of anti-CD40 antibodies. Katira et al. Do exemplify combining anti-CD40 antibodies which bind different epitopes on CD40 and which do / do not block CD40:CD40L binding.

It was well known to use of chimeric, humanized, Delimmunized, human antibodies as well as antibody fragments at the time the invention was made, as acknowledged on page 6 - 9 of the instant specification. In addition to the decreased immunogenicity of recombinant antibodies and antibody fragments, the use of the claimed antibodies and antibodies fragments were all well known and practiced at the time the invention in a wide variety of assays and methods, including detection and therapeutic modalities.

In addition, given the number of anti-CD40 antibodies at the time the invention was made, it would have been obvious to the ordinary artisan at the time the invention was made to combine anti-CD40 antibodies, including those that inhibit CD40L binding and those that do not inhibit CD40L binding to CD40 to manipulate cell interactions and responses as well as to determine structure - function relationships between CD40 and CD40L and the cells that express these antigens at the time the invention was made.

Therefore, given the referenced teachings of agonist anti-CD40 antibodies in stimulating B lymphocytes and dendritic cells, one of ordinary skill in the art would have been motivated to modify agonist anti-CD40 antibodies by providing said agonist anti-CD40 antibodies in the well known and practiced various recombinant forms and compositions encompassed by the claimed invention.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

22 Claims 7-16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fanslow et al. (U.S. Patent No. 5,801,227) (1449) AND/OR Armitage et al. (U.S. Patent No. 5,674,492) AND/OR Zhou et al. (Hybridoma 18: 471 - 478, 1999) AND/OR Caux et al. (Research in Immunology 145: 235-239, 1994) AND/OR Katira et al. (Leukocyte Typing V, Schlossman et al. (Ed.), Oxford University Press, Oxford 1995, page 554) in view of the well known use of chimeric, humanized, Delimmunized, human antibodies at the time the invention was made, as acknowledged on page 6 - 9 of the instant specification as applied to claims 1-9 and 12-16 above and further in view of

Ledbetter et al. (U.S. Patent No. 6,132,992), Chang et al. (U.S. Patent No. 6,106,835) and Heath et al. (Eur. J. Immunol. 24: 1828-1834, 1994).

Fanslow et al. (U.S. Patent No. 5,801,227) (1449) AND/OR Armitage et al. (U.S. Patent No. 5,674,492) AND/OR Zhou et al. (Hybridoma 18: 471 - 478, 1999) AND/OR Caux et al. (Research in Immunology 145: 235-239, 1994) AND/OR Katira et al. (Leukocyte Typing V, Schlossman et al. (Ed.), Oxford University Press, Oxford 1995, page 554) in view of the well known use of chimeric, humanized, Delimmunized, human antibodies at the time the invention was made, as acknowledged on page 6 - 9 of the instant specification are taught above.

These references differ from the claimed invention by not disclosing the well known use of bispecific antibodies at the time the invention was made and by not exemplifying the combination of anti-CD40 antibodies per se (other than Katira et al.).

Ledbetter et al. teach generating bispecific antibody molecules, including the CD40 specificity (see entire document, including columns 9-10). It is acknowledged that Ledbetter et al. is focused on expression vectors expressing said bispecific molecules, it is clear that these vectors and recombinant means are used for the production of said bispecific molecules (see entire document).

Chang et al. teach immunoregulatory bispecific antibody molecules which can bind different antigenic epitopes on the same antigen wherein said antibodies do bind noncompetitively without significant hindrance from each other (see entire document, including Summary of the Invention and Detailed Description of Making and Using the Invention, including column 6, lines 30-46).

Heath et al. teach monoclonal antibodies that bind murine CD40 which define distinct functional epitopes (see entire document, including Abstract and Discussion) and that this information supports the teachings of distinct cooperative epitopes on CD40, as taught by Katira et al. (See page 1833, column 1, paragraph 1).

Katira et al. teach the identification of co-operative epitopes on CD40 with anti-CD40 antibodies and combinations of anti-CD40 antibodies and that some of these antibodies block binding of CD40 to CD40L and some did not (see entire document).

Heath et al. further teach comparing the diversity of agonistic anti-CD40 antibodies, including the recognition of different epitope specificities and different requirements to generate stimulation (see Discussion, particularly page 1833, column 1, paragraph 2).

Given the recognition of different epitopes and properties of agonist anti-CD40 antibodies as well as the ability of different anti-CD40 antibodies to cooperate in achieving said agonist properties, one of ordinary skill in the art at the time the invention was made would have been motivated to combine said agonist antibodies, with the knowledge that such agonist antibodies would include those antibodies that block and do not block CD40:CD40L binding and that such combinations of agonist anti-CD40 antibodies would cooperate in achieving agonistic effects. Further, one of ordinary skill in the art at the time the invention was made would have been motivated to combine said agonist anti-CD40 antibodies in a convenient formulation, that is, bispecific antibodies, wherein said bispecific antibodies bind different epitopes on CD40. Given the teachings of the prior art references, the ordinary artisan would have an expectation of success that agonist anti-CD40 antibodies would operate on a variety of CD40-bearing cells at the time the invention was made, including various antigen presenting cells, encompassed by the claimed invention.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

23. No claim allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
August 29, 2002